REMARKS

Drawings

In the Office Action mailed April 1, 2003, the Examiner states that formal drawings will be required when the application is allowed. Applicant submits that formal drawing will be submitted.

The 35 U.S.C. §102 Rejection

Claims 1, 5 and 8 are rejected under 35 U.S.C. §102(b) as being anticipated by **Dworkin** et al. (1995, J. Biol. Chem., vol. 270). The rejection is respectfully traversed.

Dworkin et al. teach the cloning of S-layer protein from a type B *C. fetus* strain and disclose conservation of the sap homologs between type A and type B *C. fetus*. **Dworkin** et al. teach a *C. fetus* strain 82-40 LP3, and the Examiner asserts that 82-40 LP3 is a derivative of strain 23D as it differs from strain 23D by expressing an additional antigen (a 127 kDa protein) that is heterologous to strain 23D. The Examiner further asserts that

Figures 4-7 provide support that 82-40 LP3 is a mutant strain of 23D.

Applicant submits that the assertion of 82-40 LP3 as a derivative or mutant of strain 23D is not supported by the data disclosed in **Dworkin** et al. Table 1 of **Dworkin** et al. only teaches that 82-40 LP3 is a spontaneous variant of 82-40 LP. **Dworkin** et al. do not teach or suggest any relationship between strain 82-40 LP (or 82-40 LP3) and strain 23D. Although 82-40 LP3 and 23D are both serotype A *C. fetus* strains, that does not necessarily follow that 82-40 LP3 is derived from strain 23D. Undoubtedly strain 23D is not the only type A *C. fetus*, and there are many other type A *C. fetus* strains that are not related to or derived from strain 23D. One of ordinary skill in the art would not reasonably conclude that 82-40 LP3 is derived from strain 23D simply because they are both type A *C. fetus*. Similarly, Figures 4-7 only show the presence or absence of sequences common to type A or type B *C. fetus* in the *C. fetus* strains examined in **Dworkin** et al. Figures 4-7 only show that 82-40 LP3 and 23D are both serotype A *C. fetus*. Without further data, Figures 4-7 do not teach or suggest 82-40 LP3 is derived from strain 23D.

The Examiner shifts the burden to Applicant to provide proof that the claimed product is different from that in prior art. Applicant submits that strain 82-40LP was isolated in 1981 from an infected human (**Dworkin** et al., J. Bacteriol. 177:1734 (1995)), whereas strain 23D was isolated in 1975 from cattle (**McCoy** et al., Infect. Immun. 11:517 (1975)).

The Examiner also contends that **Dworkin** et al. anticipates the instant invention because **Dworkin** et al. teach a *C. fetus* strain expressing a heterologous surface associated protein in the S-layer (see Table 1). Table 1 lists a type A spontaneous variant *C. fetus* strain 82-40 LP3 that expresses a 127 kDa S-layer protein in addition to the 97 kDa protein expressed by wild type *C. fetus* strain 23D. However, neither Table 1 nor elsewhere in **Dworkin** et al. provides any support that this 127 kDa S-layer protein is heterologous to strain 82-40 LP3. In contrast, in view of the fact that "type A cells possess eight *sapA* homologs that encode 97 kDa or larger S-layer protein" (**Dworkin** et al., page 15093, right column, second paragraph, third sentence), a reasonable explanation for the 127 kDa S-layer protein is that it is derived from one of the *sapA* homologs in strain 82-40 LP3, i.e. it is not heterologous to strain 82-

40 LP3. In other words, one of ordinary skill in the art would not reasonably conclude that the 127 kDa S-layer protein is heterologous to strain 82-40 LP3 simply because the 127 kDa protein is not expressed by wild type *C. fetus.*

In conclusion, **Dworkin** et al. do not provide any support for the assertion that 82-40 LP3 is derived from strain 23D. Neither do **Dworkin** et al. provide any support for the assertion that the 127 kDa S-layer protein is heterologous to strain 82-40 LP3. In view of the above remarks, **Dworkin** et al. do not teach or suggest each and every aspect of the present invention. Hence, **Dworkin** et al. do not anticipate claim 1 of the present invention. Accordingly, Applicant respectfully requests that the rejection of claims 1, 5 and 8 under 35 U.S.C. §102(b) be withdrawn.

The 35 U.S.C. §112 Rejection

Claims 1, 5, 8-13 and 15-17 are rejected under 35 U.S.C. §112, first paragraph, for lack of deposit. The rejection is respectfully traversed.

The Examiner rejects the claims for not positively recite the deposited strains. Applicant submits that claims 1, 10, 12 and 15 have been amended to positively recite the ATCC deposited strains as helpfully suggested by the Examiner. In view of the deposits and amendments, Applicant respectfully requests that the rejection of claims 1, 5, 8-13 and 15-17 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 1, 5, 8-13 and 15-17 are rejected under 35 U.S.C. §112, first paragraph, for lack of written description. The rejection is respectfully traversed.

The Examiner rejects the claims for not positively recite the deposited strains. Applicant submits that claims 1, 10, 12 and 15 have been amended to positively recite the ATCC deposited strains as helpfully suggested by the Examiner. In view of the deposits and amendments described above, Applicants submit that the written description requirement has been satisfied in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Accordingly, Applicants respectfully request that the

rejection of claims 1, 5, 8-13 and 15-17 under 35 U.S.C. §112, first paragraph, be withdrawn.

New Grounds of Rejection

Claims 11, 12 and 13 are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The rejection is respectfully traversed.

The Examiner contends that claim 11 is directed to a mutant strain with a heterologous protein sequence inserted into the only *sapA* coding sequence, thus disrupting the overall reading frame of the DNA for the *sapA* encoded protein. With such disruption, no surface chimeric protein would be produced, and the claimed method of immunization is not enabled because no surface heterologous protein is expressed by the mutant. Applicant respectfully disagrees.

Example 19 of the present invention teaches that a *sapA* homologs can be altered so that the central portion of the homolog-specific region is replaced by a DNA cassette encoding a heterologous antigen. The replacement is constructed so that the

resulting recombinant S-layer protein is a tripartite chimera consisting of the N-terminal LPS-bining domain of the S-layer protein, a central region composed of the heterologous antigen, and a C-terminal segment containing the S-layer protein secretion signal. This protein would be able to be secreted from the cell by means of the C-terminal secretion signal and into the LPS on the *C. fetus* cell surface, thereby exposing the heterologous antigen to the host immune system (page 25, line 25 to page 26, line 3). The present specification also teaches the C-termini of *C. fetus* S-layer proteins contain conserved sequences and secondary structures that are candidates for secretion signals (Example 18, page 23, line 26 to page 24, line 22). Therefore, in view of the present disclosure, Applicant submits that one of ordinary skill in the art would readily utilize standard genetic engineering techniques to construct a tripartite chimera consisting of the N-terminal LPS-bining domain of the S-layer protein, a central region composed of the heterologous antigen, and a C-terminal segment containing the S-layer protein secretion signal. Applicant submits that it is highly unlikely that the overall reading frame would be disrupted by the genetic engineering because in-frame insertion that maintains the overall reading frame

can be accomplished without difficulties under the current state of the art.

In view of the present disclosure and the state of the art of genetic engineering, Applicant submits that the scope of the claimed *C. fetus* mutant and the method of use is commensurate with the enablement provided. No undue experimentation is required to practice the claimed invention. Accordingly, Applicant respectfully requests that the rejection of claims 11, 12 and 13 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 1, 10, 11 and 12 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The rejection is respectfully traversed.

Claims 1, 10 and 12 are rejected for reciting ATCC designation in parenthetical notations. Applicant submits that claims 1, 10 and 12 have been amended to positively recite the ATCC deposited strains. Consequently, Applicant submits that the amended claims have distinctly pointed out and claimed the subject matters of the invention. Accordingly, Applicant respectfully

requests that the rejection of claims 1, 10 and 12 under 35 U.S.C. §112, second paragraph, be withdrawn.

The Examiner rejects claim 11 for inserting a heterologous protein sequence into the only *sapA* coding sequence, thus disrupting the overall reading frame of the DNA and preventing surface expression of the chimeric protein. As discussed above, Applicant submits that it is highly unlikely that the overall reading frame would be disrupted by genetic engineering because in-frame insertion that maintains the overall reading frame can be accomplished without difficulties under the current state of the art. Claim 11 has been amended to recite inserting a DNA cassette encoding a heterologous protein into the coding sequence of a *sap*A homolog, resulting in surface expression of a chimeric protein comprising a 5' LPS-binding region of said *sap*A homolog, said heterologous protein and a 3' secretion signal region of said *sap*A homolog. Applicant submits that claim 11 has been amended to distinctly claim the subject matter of the invention. Accordingly, Applicant respectfully requests that the rejection of claim 11 under 35 U.S.C. §112, second paragraph, be withdrawn.

This is intended to be a complete response to the Final Office Action mailed December 29, 2003. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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